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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,271	02/06/2004	Takayuki Asahara	US-107	4145

38108 7590 07/24/2007

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,271	ASAHARA ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/8/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-6,9 and 12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-8, 10-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response, filed 1/8/2007, are acknowledged. Claim 7 has been amended. New claims 10-18 have been added.

Election/Restrictions

Newly submitted claims 11-18 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 11-18 are part of Group V, as set forth in the restriction requirement set forth on 8/8/2006. As stated previously, Inventions IV and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). In the instant case, the bacterium of Invention IV can be used to raise antibodies.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-18 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's response (filed 4/6/2007) to the notice of non-responsive amendment filed 3/29/2007, is noted.

Applicant argues:

1. That the examiner disregarded the requirements of "Election by Original Presentation" by alleging that amended claims 7-8 did not read on the elected invention because they recited only a disrupted form of the gene. Applicant asserts that the disrupted form of the gene was encompassed by the original claim 7. The claim language in question reads "wherein a gene on said bacterium's chromosome has the same nucleotide sequence as the DNA of claim 1, or which has homology to the DNA of claim 1 to such an extent that homologous recombination results in disruption of said DNA, thereby suppressing expression of the gene." Applicant asserts that because of the word "or" there are two alternatives encompassed; a gene having SEQ ID NO:1 and a gene which is disrupted due to homologous recombination. It is applicant's contention that

the examiner examined both of these embodiments, and applicant suggests that the rejection under 35 USC 112, second paragraph (stating that the embodiment being claimed would require the gene to be disrupted) is evidence of this.

2. That election by original presentation cannot be instituted since there was never any restriction between the disrupted and undisrupted form of the gene. Applicant suggests that, because both embodiments were examined, they did not elect the undisrupted form of the gene.

3. That the language used in the notice of non-compliance did not properly set forth the basis for a new restriction requirement, denying applicants a fair opportunity to assess and respond to the restriction requirement.

Regarding argument 1, applicant's assertions are incorrect. The claimed bacteria were required to have the DNA of SEQ ID NO:1, or they were required to have a gene that has homology to such an extent that homologous recombination results in disruption of the DNA. This statement does not say that the gene is disrupted by homologous recombination. The statement is a measure of the homology to SEQ ID NO:1. If the gene in question had very low homology, no recombination could occur, whereas if it had high homology, recombination could occur. This is not to say that it did occur, but that the gene was homologous enough to SEQ ID NO:1 that it could. This is supported by the specification. Paragraph 0044 states that the bacterium of the invention "can be constructed by disrupting *gtfA* or *manC*, or a homologue thereof having homology to either one of them in such a degree that homologous recombination should be caused with either one of them." The specification goes on to say that such homology is "preferably 90% or more, more preferably 95% or more, particularly preferably 99% or more." Clearly, the statement is meant to reflect the degree of homology of the *gtfA* homolog. The amended claims require the gene to be disrupted, which is the opposite of what was originally claimed. Applicant's assertion that the 112 (2) rejection is evidence that both embodiments were examined is also incorrect. In fact, it is evidence of the opposite. The rejection pointed out that it appeared, from the specification, that the invention disclosed was a bacterium with a disrupted gene. The rejection went on to state "however, according to the claims, the bacterium should have *gtfA*, which would therefore not be disrupted." If the examiner considered disrupted genes as part of the invention, the rejection would not make sense. The rejection was based on the fact

that the claimed invention was different from the invention disclosed in the specification. The rejection clearly states that the claim requires the presence of undisrupted *gtfA*.

Regarding argument 2, it is true that there was not a restriction between the disrupted and undisrupted form of the genes, but this is because the claims did not read on the disrupted form of the genes. Only the amended claims read on the disrupted form. Therefore, applicant's originally presented invention was the undisrupted form. If the newly amended claims had been present at the time the restriction requirement was made, they would have been separated from the elected invention. As stated in the notice of non-responsive amendment, withdrawal of the non-elected claims would have resulted in there being no pending claims. According to MPEP 821.03, if all claims drawn to the elected invention are cancelled, leaving only non-elected claims, the amendment is non-responsive.

Regarding argument 3, the notice of non-responsive amendment clearly set forth the reasons that the new invention was found to be independent or distinct. The notice clearly stated that the original claims were drawn to bacteria with the sequence of SEQ ID NO:1 and that the amended claims were drawn to bacteria with a disrupted, non-functional version of this gene. The notice further stated "the invention of the amended claims is independent from the originally elected invention because these bacteria are unconnected in design, operation, and effect." A new restriction requirement was not being set forth, as applicant had already elected an invention, and was presenting claims to a new invention subsequent to the first office action.

However, in the interest of furthering prosecution and customer service, the new invention (a bacterium having a disrupted form of SEQ ID NO:1) is being examined as set forth in the amended claims.

Claims 1-18 are currently pending. Claims 1-6, 9, and 12-18 are withdrawn from consideration as being directed to a non-elected invention. Claims 7-8 and 10-11 are currently under examination.

Claim Rejections Withdrawn

The rejection of claims 7-8, under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 7 as being rendered vague and indefinite by the phrase "A methanol-utilizing bacterium having an ability to reduce production of a polysaccharide, wherein a gene on said bacterium's chromosome has the same nucleotide sequence as the DNA of claim 1, or which has homology to the DNA of claim 1 to such an extent that homologous recombination results in disruption of said DNA, thereby suppressing expression of the gene," is withdrawn in light of applicant's amendment thereto.

The rejection of claims 7-8, under 35 U.S.C. 102(b) as being anticipated by NCIMB Culture Collection (NCIMB Culture Collection Online Catalog, accessed 9/21/2006, http://www.ncimb.co.uk/results.php?parent+culture), is withdrawn in light of applicant's amendment thereto.

New Claim Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to isolated methanol-utilizing bacteria that have a reduced ability to produce a polysaccharide, wherein the bacteria have a gene on their chromosome that is disrupted so that expression of the gene is suppressed. The gene is to be selected from a DNA comprising the nucleotide sequence of SEQ ID NO:1 and a DNA which is hybridizable with a DNA comprising the nucleotide sequence of SEQ ID NO:1 under stringent conditions comprising 1x SSC, 0.1% SDS at 60°C. It is noted that the claims recite "stringent conditions"

comprising 1x SSC, 0.1% SDS at 60°C. Because of the use of the word "comprising," the claims encompass any additional hybridization conditions. In addition, the mere fact that a piece of DNA hybridizes to SEQ ID NO:1 does not mean that said DNA encodes a protein related to *gtfA*. A probes could fully hybridize to SEQ ID NO:1, but said probe would not constitute a gene and disruption of said DNA would not necessarily alter polysaccharide production. The specification specifically discloses SEQ ID NO:5 and 6 which are examples of this. Therefore the claims encompass all bacteria which are capable of utilizing methanol in any way, that have any gene related at all to *gtfA*, and to production of any molecule other than polysaccharides. Furthermore, the specification specifically envisions DNA having as low as 70% homology with SED ID NO:1.

The specification discloses a *Methylophilus methylotrophus* strain that has a disruption in the gene (*gtfA*) that has the sequence of SEQ ID NO:1. This bacterium meets the written description provision of 35 USC 112, first paragraph. However, the claims are drawn to a vast genus of bacteria that are capable of utilizing methanol in any way, that have any gene related at all to *gtfA*. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

The art shows that there are many bacteria that utilize methanol, and many unrelated bacteria that have *gtfA*, such as *Streptococcus mutans* and *Mycobacterium avium* (Russell *et al.*, Infect. Immun., 56:2763-2765, 1988; Eckstein *et al.*, Microbiol. 149:2797-2807, 2003). These genes encode glycosyltransferases that vary from between species. Gunji *et al.* (US Patent 7,223,572, filed 4/2000) disclose a strain of *Methylophilus methylotrophus* that was deposited under the accession number FERM BP-7112. According to the instant specification, this strain has a disrupted *gtfA* gene. While the art and specification do show one strain of bacteria that meet the limitations of the claims, they do not show which mutations, short of complete deletion, would lead to suppression of expression of *gtfA* or SEQ ID NO:1, let alone an unknown homolog or complementary strand of SEQ ID NO:1, nor do the art or specification show what level of suppression is enough to allow the only stated utility, which is production of unknown molecules (other than polysaccharide).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with

> reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Therefore, only a *Methylophilus methylotrophus* strain that has a disruption in the gene (*gtfA*) that has the sequence of SEQ ID NO:1, but not the full breadth of the claims meets the

written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement.

Moreover, DNA that hybridizes to the DNA sequence that encodes a protein is known as complementary DNA. "Complementary" is routinely used in the art to describe the opposite strand of a given DNA sequence (p. 115, col. 1, Lodish *et al.*, Mol. Cell Biol., 3rd ed. Scientific American Books, NY, 1995), therefore the claim reads upon DNA that is antisense to the coding strand of *gtfA*, or the antisense of SEQ ID NO:1. It is well known that antisense sequences do not encode products related to the sense strand, for example, the 5'- 3' directionality is reversed, and therefore each codon triplets is read in the reverse orientation (encoding a different amino acid in most instances) and the N and C terminal of the encoded product is reversed. Applicant has not provided any guidance or working examples to show any bacteria that contain a gene that is antisense to *gtfA*, nor has applicant shown that disruption of such a gene would create a bacterium that has the utility of producing any particular unknown target molecule. Applicant has not provided any potential means of using such an unrelated gene, or any description of the structure or function of such the product produced by said gene.

Claims 7-8 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected claims are drawn to isolated methanol-utilizing bacteria that have a reduced ability to produce a polysaccharide, wherein the bacteria have a gene on their chromosome that is disrupted so that expression of the gene is suppressed. The gene is to be selected from a DNA comprising the nucleotide sequence of SEQ ID NO:1 and a DNA which is hybridizable with a DNA comprising the nucleotide sequence of SEQ ID NO:1 under stringent conditions comprising 1x SSC, 0.1% SDS at 60°C.

Breadth of the claims: Because of the use of the word "comprising," the claims encompass any hybridization conditions. In addition, the mere fact that a piece of DNA hybridizes to SEQ ID NO:1 does not mean that said DNA encodes a protein related to *gtfA*. A probes could fully hybridize to SEQ ID NO:1, but said probe would not constitute a gene and disruption of said DNA would not necessarily alter polysaccharide production. The specification

specifically discloses SEQ ID NO:5 and 6 which are examples of this. Therefore the claims encompass all bacteria which are capable of utilizing methanol in any way, that have any gene related at all to *gtfA*, and to production of any molecule other than polysaccharides. Furthermore, the specification specifically envisions DNA having as low as 70% homology with SED ID NO:1.

Guidance of the specification/The existence of working examples: The specification discloses a *Methylophilus methylotrophus* strain that has a disruption in the gene (*gtfA*) that has the sequence of SEQ ID NO:1. The *gtfA* gene encodes a galactosyl-1-phosphate transferase; however, the specification does not provide any guidance regarding which portions of the gene are necessary for said activity, nor is there any information regarding which homologs are capable of said activity and there is no information regarding which mutations, short of complete deletion, would lead to suppression of expression of *gtfA* or SEQ ID NO:1, let alone an unknown homolog or complementary strand of SEQ ID NO:1.

State of the art: The art shows that there are many bacteria that utilize methanol, and many unrelated bacteria that have *gtfA*, such as *Streptococcus mutans* and *Mycobacterium avium* (Russell *et al.*, Infect. Immun., 56:2763-2765, 1988; Eckstein *et al.*, Microbiol. 149:2797-2807, 2003). These genes encode glycosyltransferases that vary from between species. Gunji *et al.* (US Patent 7,223,572, filed 4/2000) disclose a strain of *Methylophilus methylotrophus* that was deposited under the accession number FERM BP-7112. According to the instant specification, this strain has a disrupted *gtfA* gene.

Further, with regard to genes comprising DNA that hybridizes to SEQ ID NO;1, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie *et al.* (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (column 1, page 1306). Bowie *et al.* further teach that while it is known that many amino acid substitutions are possible in any given

protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess *et al.* (J. of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar *et al.* (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, polynucleotides with more than 30% dissimilarity to the polynucleotides of SEQ ID NO:1 that maintained the characteristics of the polypeptides encoded by SEQ ID NO:1 could not be predicted. Additionally, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, column 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, column 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, column 3). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, column 2). Most features predicted with an accuracy of greater than 70% are of structural nature and, at best, only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399, paragraph bridging columns 2 and 3). The reference finally cautions that

although the current methods seem to capture important features and explain general trends, 30% of those features are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, paragraph bridging cols 1 and 2). Clearly, given not only the teachings of Bowie *et al.*, Lazar *et al.*, and Burgess *et al.* but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, the claimed polynucleotides could not be predicted based on homology to SEQ ID NO:1. Clearly, it could not be predicted that a polynucleotide, or a variant, that encodes a protein that shares only partial homology with a disclosed protein or that a protein that is encoded by a "variant" of a given SEQ ID NO: will function in a given manner. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use bacteria with disruptions in the polynucleotides of SEQ ID NO:1.

Moreover, neither nor do the art or specification show which mutations, short of complete deletion, would lead to suppression of expression of *gtfA* or SEQ ID NO:1 in any particular species of bacteria, let alone an unknown homolog or complementary strand of SEQ ID NO:1, nor do the art or specification provide any guidance regarding what level of suppression of said gene is enough to allow the only stated utility, which is production of unknown molecules (other than polysaccharide).

Therefore, in view of the lack of support in the art and specification, it would require undue experimentation on the part of the skilled artisan to make and use the invention as claimed; consequently, the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is rendered vague and indefinite by the phrase "wherein the gene is selected from the group consisting of: (a) a DNA comprising the nucleotide sequence of SEQ ID NO:1; and (b)

a DNA which is hybridizable with a DNA comprising the nucleotide sequence of SEQ ID NO:1 under stringent conditions comprising 1 x SSC, 0.1% SDS at 60°C." DNA that hybridizes with SEQ ID NO:1 would not constitute a gene. A DNA that is only a few bases long could hybridize completely to a DNA with the sequence of SEQ ID NO:1, but would not constitute a full gene. In addition, according to the specification, SEQ ID NO:1 is the full length of the *gtfA* gene. Therefore, a DNA that contained bases in addition to *gtfA* would not necessarily constitute *a* gene.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-8 and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Gunji *et al.* (US Patent 7,223,572, 5/2007). US Patent 7,223,572 was filed as the national stage of PCT/JP00/02295 which was published as WO00/61723 on 10/19/2000. WO00/61723 was published in Japanese and will be provided when a translation becomes available. Because US Patent 7,223,572 was filed as the national stage of PCT/JP00/02295, the specification of the cited US Patent is a translation of the WO document and the US Patent is being used until the Japanese translation becomes available.

The instant claims are drawn to isolated methanol-utilizing bacteria that have a reduced ability to produce a polysaccharide, wherein the bacteria have a gene on their chromosome that is disrupted so that expression of the gene is suppressed. The gene is to be selected from a DNA comprising the nucleotide sequence of SEQ ID NO:1 and a DNA which is hybridizable with a DNA comprising the nucleotide sequence of SEQ ID NO:1 under stringent conditions comprising 1x SSC, 0.1% SDS at 60°C (claim 7), wherein the bacterium is a *Methylophilus* bacterium (claim 8).

Gunji *et al.* disclose a strain of *Methylophilus methylotrophus* that was deposited under the accession number FERM BP-7112 (see page 23, lines 32-41). According to the instant

specification (paragraph 0056), this strain is a specific example of a strain "according to the second embodiment of the present invention." The specification further states, "The bacterium according to the second embodiment of the present invention can be constructed by disrupting *gtfA* or *manC*... so that the gene product thereof should not normally function," (paragraph 0044). In the absence of evidence to the contrary, based on the information provided in the instant specification, the strain deposited under the accession number FERM BP-7112 meets the limitations of the claims.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian Gangle
AU 1645

ROBERT A. ZEMAN
PRIMARY EXAMINER